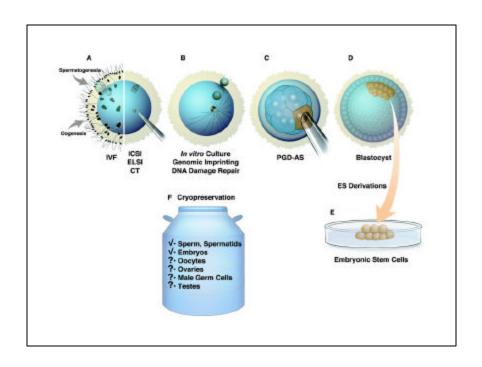


# Safeguarding ART:ARTsilomar?

- Why Now? Why Asilomar?
  - Germline Transfer, Egg Commerce, ESCs, Cloning
  - Consensus Among Knowledgeable Stakeholders
- Facts: nomenclature, identify knowledge gaps;
- Accepted, Exp'tal &Unwarranted: Safeguarding of ART, hESC and cloning initiatives;
- Education:
  - Clear communication;
  - foster on-going ELSI conversations;
  - Enhance Genetic Counseling



#### **ICSI-ART Facts Needed:**

To Reduce Any Risks, and To Weigh Risk/Benefit Ratio

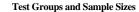
- Sperm Selection? Sperm Sanitation?
- Sperm Primed for Nucleus Decondensation?
  - Membrane SNAREs
  - Perinuclear Theca
  - Acrosome Enzymes
  - Sex Chromosome Position
- Mitochondria Destruction and Pregnancy?
- Improved Prenatal Screens?
  - Mitochondria
  - Genomic Imprinting
  - Foreign DNA
- ICSI Children, Grandchildren, Great-grandchildren?
  - Health, Psychology, Reproductive Normalcy
- Consequences of Our First Environment

## Evidence Based ART: Global Clinical-Translational Initiative

- Clinical, Primate and Mice Outcome Studies
- •Identify and Minimize Any ART Risks.
- •Weigh the Risk to Benefit Ratio.

#### **Outcomes Investigations of Macaque ART**

- Identify outcomes from ICSI or ELSI offspring in the relevant model that exhibits complex social behaviors;
  - •Propagate Twenty-four Monkeys Using Three Different ART Methods:
    - •1. ICSI Using Ejaculated Sperm,
    - •2. ELSI Using Élongated Spermatids Retrieved From the Same Male on Same Day With the Same Clutch of Eggs, As Well As Others, &
    - •3. Al (Artificial Insemination) With Identical & Different Spem.
- Two generations of ICSI rhesus offspring will be born before 2007, and three generations by 2012—long before children of ICSI;
- · Verify the safety of ICSI and ELSI;
- Improve the techniques further; and
- Provide reassurance for ART practitioners, their infertile patient couples, and especially their ultimate patients--- the children.



	Control	Embryo Split	ICSI	IVF
Females	5	2	2	4
Males	10	3	2	0

### **Germline Gene Transfer**

- ➤ Germ Vs. Somatic Cells: WRONG!!
- Assisted Reproductive Technologies (ART): Gametes, Embryos
- > Transgenesis
- > Gene Therapy, Enhancement: *In Utero*, Biohazard, Bioterror
- Stem Cells and Cloning: Embryonic Stem (ESC); Embryonic Germ Cells (EGC)

NICHD Challenge-ELSI One Stop

#### **Germline Gene Transfer**

- > Nuclear DNA
  - >ATGC
  - Fifth Nucleotide: 5-methyl-C, parent of origin imprint
  - >Transgenerational Imprint Transmission
- Mitochondrial DNA
- > Exogenous DNA/RNA:
  - **≻**Gene Therapy Vector,
  - ➤Infection: viral, bacteria, prion
- > Centrosomes: Microtubule Organizing Center
- > Endomembranes: ER, Golgi, etc.
- > Cytoplasm; RNA
- > Other Inherited Components?

#### **Germline Gene Transfer**

Where Are We?Where Can We Go? Why?Where Should We Go? Do We Know What We Don't Know?

- > Overcoming Infertility: Intentional vs. Unintentional
  - ➤Infertility Gene Transmission
  - >mtDNA Heteroplasmy
  - ➤'Immaculate Infection?' Viral transmission during ART, cryobanking, embryo culture, Skewed X-inactivation
- > Preimplantation Genetic Diagnosis, Aneuploid Screening
  - ➤ Huntington's, CF, SCD, DMD, X errors
  - ➤ Male Germ Cell Transplantation: Transgenic Sperm
- > Human Embryonic Gene Therapy vs Enhancement
- > Embryonic Stem Cells and Cloning: Germline Entry
- > Gametes After Gene Therapy
- > Transgenic Primate Models

# GRATEFUL ACKNOWLEDGEMENTS TO: NICHD AND NCRR

#### Update acknowledgements

Gerald Schatten, PhD John Bassir, MS Anthony Chan, DVM, PhD Kowit-Yu Chong, PhD Tanja Dominko, DVM, PhD Nancy Duncan, MS Michelle Emme Laura Hewitson, PhD Ethan Jacoby, BS Kay Larkin, PhD Crista Martinovich, BS Bryan McVay, MS Michelle Miller, MS Ricardo Moreno, PhD Kevin Mueller, BS Evelyn Neuber, PhD Chris Payne, BS João Ramalho-Santos, PhD

Gabriel Sanchez-Partida, PhD

Calvin Simerly, PhD Peter Sutovsky, PhD Tonya Swanson, BS Diana Takahashi, MS Jaclyn Vidgoff, PhD

Division of Lab Animal Medicine John Fanton, DVM Darla Jacob Kevin Grund Sam Siemon

Infant Primate Research Lab @ UW NICHD Human Develop. Cnt & NCRR WaRPRC Gene Sackett, PhD

University of Birmingham, UK Justin St. John, PhD